Drawings

The Examiner stated that formal drawings and photographs have been submitted which fail to comply with the 37 C.F.R. §1.84. The Examiner stated that please see the form PTO-948 previously sent in Paper No. 7. The Examiner stated that applicant is reminded to change the Brief Description of the Drawings in accordance with these changes.

In response, applicants will provide formal drawings upon the indication of allowable subject matter.

35 U.S.C. §112, first paragraph- claim 33

The Examiner objected to the specification and rejected claim 33 under 35 U.S.C. §112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention essentially for the reasons set forth in Paper No. 7.

The Examiner stated that applicant's arguments in conjunction with Exhibits A-C, filed 5/4/98 (Paper No. 9), have been fully considered but are not found convincing.

The Examiner stated that applicant argues that the use of aerosol, oral, topical carriers for delivering therapeutic effective amounts of compositions are known in the art. The Examiner stated that with respect to treating disorders associated with the claimed disorders, applicant provides Exhibits A-C.

The Examiner stated that however, the nature of pharmaceutical compositions relied upon by these Exhibits differ dramatically in their pharmacokinetics properties than the factor IX. The Examiner stated that applicant's evidence does not rely upon proteins such as factor IX, which would require the appropriate conformation and, in turn, access to the vascular system to be

therapeutically effective. The Examiner stated that applicant has not provided sufficient guidance and direction nor objective evidence that the skilled artisan can deliver a therapeutic effective amount of a protein, even a chemically inactivated protein, such as the instant factor IX in an aerosol, oral or topical carrier in treating ischemic disorders. The Examiner stated that Ischemia comprises treating vascular disorders and it would not be predictable that one could deliver a therapeutic effect amount in such disorders other than intravascular routes of administration. The Examiner stated that in the absence of objective evidence to the contrary, aerosol, oral and topical carriers and means for delivery for proteins such as the instant factor IX are not enabled for treating ischemia. The Examiner stated that applicant's arguments are not found persuasive.

In response, applicants respectfully traverse the Examiner's above objection and rejection. Applicants contend that claim 33 which recites "the method of claim 32, wherein the pharmaceutically acceptable carrier comprises an aerosol, intravenous, oral or topical carrier" is fully enabled. Applicants respectfully contend that in addition to intravenous carriers, the use of aerosol, oral and topical carriers for delivering therapeutic effective amounts of compositions are known in the art.

Nevertheless, applicants, without conceding the correctness of the Examiner's position but to expedite the prosecution of the subject application, have deleted references to aerosol, oral and topical carriers from claim 33. Since the amended claim does not contain these terms, applicants believe that the amended claim has rendered the above objection and rejection moot. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw the rejection.

35 U.S.C. §103(a)

The Examiner rejected claims 29-38 under 35 U.S.C. §103 as being unpatentable over Moller et al. (CA 2,141,642) in view of standard methods of inactivation as acknowledged on page 17 of the instant specification and in view of known ischemic disorders as acknowledged on page 16 of the instant specification essentially for the reasons of record set forth in Paper No. 7.

The Examiner stated that applicant's arguments, filed 5/4/98 (Paper No. 9), have been fully considered but are not found convincing. The Examiner stated that applicant argues that the amended claim 29 obviates the previous rejection. The Examiner stated that applicant argues that Moller et al. teaches away from the use of chemically modified factor IX. The Examiner stated that applicant relies upon pages 4-5 and 10 of Moller et al., which discloses that "proteolytic fragments are not modified and that "fragments shouldn't be chemically modified" and that their invention is an "avoidance of chemical modification of factor IX fragments.

The Examiner stated that however, the instant claims are not drawn to chemically modified fragments, but rather chemically inactivated factor IXa. The Examiner stated that as known in the art at the time the invention was made and disclosed in this reference, factor IX has an important role in hemostasis. The Examiner stated that the key to Moller's invention was determining fragments that do not have coagulation activity and therefore avoid the use of chemical inactivation. The Examiner stated that however, the instant claims are not drawn to the small fragments that do not have coagulation activity relied upon by Moller. The Examiner stated that in contrast, the instant factor IXa was known and was expected to have coagulation activity. The Examiner stated that therefore, to employ the instant factor IXa as an antagonist, the ordinary artisan would have recognized the requirement to inactivate said factor IXa;

otherwise it would have had coagulation activity. The Examiner stated that such coagulation activity runs contrary to the desired inhibitory effects. The Examiner stated that furthermore, event though Moller's invention was drawn to determining certain fragments with inhibitory effects, this does not discount that the ordinary artisan was motivated to antagonize thrombosis with factor IX-derived fragments. The Examiner stated that to avoid the coagulation activity of such fragments, such as factor IXa; it would have been obvious and necessary to inactivate such coagulation properties to be used as an inhibitory agent. The Examiner stated that such inactivation including chemically inactivation was known and practiced at the time the invention was made, as set forth in the last Office Action and acknowledged by applicant.

In response, applicants respectfully traverse the Examiner's above rejection for the following reasons.

1. The Examiner states that to employ the instant factor IXa as an antagonist, the ordinary artisan would have recognized the requirement to inactivate said factor IXa; otherwise it would have had coagulation activity.

Applicants point out that when applying 35 U.S.C. §103, the references must be viewed without the benefit of impermissible hindsight afforded by the claimed invention. See M.P.E.P 2143. Applicants contend that the Examiner is using applicant's claimed invention to fill in a missing gap. Applicants contend that one skilled in the art would not have thought to use Factor IXa as a starting point because Factor IXa is the active form and thus, would have coagulation activity. Applicants contend that the Examiner is using Applicant's invention in order to arrive at the idea of starting with Factor IXa. Applicants agree that if one were starting with Factor IXa, it might be obvious that one would have to inactivate it in order to avoid coagulation activity.

However, applicants contend that it was not obvious to use Factor IXa in the first place. Moller suggests the use of Factor IX fragments that do not have coagulation activity. Thus, this would not suggest the use of Factor IXa because it has coagulation activity. Applicants contend that the Examiner is making an impermissible leap because based on the teachings of Moller, the use of Factor IXa is not suggested.

Furthermore, Moller teaches away from chemical modification. Specifically, page 4 of Moller says "not chemically modified." Therefore, even if Moller had suggested Factor IXa as a starting point (which it does not), it would not suggest applicant's claimed invention, namely the chemical inactivation of Factor IXa.

2. The Examiner states that even though Moller's invention was drawn to determining certain fragments with inhibitory effects, this does not discount that the ordinary artisan was motivated to antagonize thrombosis with factor IX-derived fragments.

Applicants respectfully disagree. Applicants point out that the fact that the claimed invention is within the capabilities of one or ordinary skill in the art is not sufficient by itself to establish prima facie obviousness without some objective reason to combine the teachings of the references. See M.P.E.P. 2143.01. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art suggests the desirability of the combination. In re Mills, 916 F2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990) Applicants contend that there is nothing in Moller which would suggest to one skilled in the art that factor IXa could be used without having coagulation activity. Thus, based on Moller, one skilled in the art would not have been motivated to antagonize thrombosis with Factor IXa.

Accordingly, in view of the foregoing, applicants contend that

these remarks obviate the above objections and rejections and respectfully request that the Examiner reconsider and withdraw the rejections.

Summary

In view of the foregoing remarks, applicants respectfully request that the above grounds of rejection be reconsidered and withdrawn and earnestly solicit allowance of Claims 29-38.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

No fee, other than the $190.00 fee for a two-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

John P. White
Registration No. 28,678
Attorney for Applicants
Cooper & Dunham, LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400